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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,984	11/20/2003	Walter Newman	3258.1008-001	8906

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EXAMINER

HADDAD, MAHER M

ART UNIT PAPER NUMBER

1644

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/717,984

Applicant(s)

NEWMAN, WALTER

Examiner

Maher M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 5/10/06.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 8/23/06, is acknowledged.
2. Claims 23-42 are pending and under examination in the instant application as they read on a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade comprising administering to a composition comprising an antibody that binds to HMGB polypeptide or a biological active fragment thereof and an agent, wherein the antibody binds to SEQ ID NO: 1, 5 and 23 species and the condition is rheumatoid arthritis and sepsis as the species.
3. Applicant's IDS filed 5/10/06, is acknowledged, however, references A2-A5 and C1-C2 were crossed out because they are duplicate of the references cited on the 892 Form mailed 4/21/06. Further only the English abstract of references B6 and B9 were considered.
4. In view of the amendment filed on 8/23/06, only the following rejections are remained.
5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
6. Claim 37 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "human antibody" claimed in claims 37, represents a departure from the specification and the claims as originally filed for the same reasons set forth in the previous Office Action mailed 4/21/06.

Applicant's arguments, filed 8/23/06, have been fully considered, but have not been found convincing.

Applicant submits that various techniques for generating human antibodies were well known in the art at the time of the invention. Accordingly, Applicant concludes that the specification and the skill and knowledge in the art at the time of the invention provide sufficient written description for the claimed human antibodies.

However, knowledge in the art is not the standard for the addition of new limitations to the disclosure as filed.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 23-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,468,533 in view U.S. Pat. No. 6,677,321 for the same reasons set forth in the previous Office Action mailed 4/21/06.

Applicant's arguments, filed 8/23/06, have been fully considered, but have not been found convincing.

Applicant submits that the '321 patent teaches the use of cetyl myristoleate (CMO) and CMO compounds in combination with other compounds useful for treating inflammatory disease. Applicant argues that the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. Applicant submits that the '321 Patent does not provide any suggestion to combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. Further Applicant submits that the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide and an agent that inhibits TNF biological activity such as infliximab, etanercept and others cited in the claims. Accordingly, Applicant concludes that the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish *prima facie* obviousness.

Contrary to Applicant assertions, given that TNF inhibitors shown to be effective for short term treatment of inflammation such as RA as taught by the '321 Patent, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the TNF or anti-TNF antibody taught by the '533 patent with the infliximab or etanercept taught by the '321 patent in a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade. It is noted that the combinational therapy of a TNF inhibitor with anti-HMGB antibody is provided by the '533 patent. It is obvious to substitute one TNF inhibitor such as an anti-TNF antibody taught by the '533 patent with a specific anti-TNF antibody such as infliximab taught by the '321 patent. Obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). MPEP 2143.02.

9. Claims 23-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. 20030060410 publication in view U.S. Pat. No. 6,677,321 for the same reasons set forth in the previous Office Action mailed 4/21/06.

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Applicant's arguments, filed 8/23/06, have been fully considered, but have not been found convincing.

Applicant submits that the '321 patent teaches the use of cetyl myristoleate (CMO) and CMO compounds in combination with other compounds useful for treating inflammatory disease. Applicant argues that the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. Applicant submits that the '321 Patent does not provide any suggestion to combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. Further Applicant submits that the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide and an agent that inhibits TNF biological activity such as infliximab, etanercept and others cited in the claims. Accordingly, Applicant concludes that the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish *prima facie* obviousness.

Contrary to Applicant assertions, given that TNF inhibitors shown to be effective for short term treatment of inflammation such as RA as taught by the '321 Patent, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the TNF or anti-TNF antibody taught by the '410 publication with the infliximab or etanercept taught by the '321 patent in a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade. It is noted that the combinational therapy of a TNF inhibitor with anti-HMGB antibody is provided by the '410 publication. It is obvious to substitute one TNF inhibitor such as an anti-TNF antibody taught by the '410 publication with a specific anti-TNF antibody such as infliximab taught by the '321 patent. Obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). MPEP 2143.02.

10. Claims 23-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. 6,448,223 in view of U.S. Pat. No. 6,677,321 for the same reasons set forth in the previous Office Action mailed 4/21/06.

Applicant's arguments, filed 8/23/06, have been fully considered, but have not been found convincing.

Applicant submits that the '321 patent teaches the use of cetyl myristoleate (CMO) and CMO compounds in combination with other compounds useful for treating inflammatory disease. Applicant argues that the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. Applicant submits that the '321 Patent does not provide any suggestion to combining a TNF antagonist, such as

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infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. Further Applicant submits that the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide and an agent that inhibits TNF biological activity such as infliximab, etanercept and others cited in the claims. Accordingly, Applicant concludes that the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish *prima facie* obviousness.

Contrary to Applicant assertions, given that TNF inhibitors shown to be effective for short term treatment of inflammation such as RA as taught by the '321 Patent, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the TNF or anti-TNF antibody taught by the '223 patent with the infliximab or etanercept taught by the '321 patent in a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade. It is noted that the combinational therapy of a TNF inhibitor with anti-HMGB antibody is provided by the '223 patent. It is obvious to substitute one TNF inhibitor such as an anti-TNF antibody taught by the '223 patent with a specific anti-TNF antibody such as infliximab taught by the '321 patent. Obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). MPEP 2143.02.

11. Claims 23-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al in view of U.S. Pat. 6,448,223 and U.S. Pat. No. 6,677,321 for the same reasons set forth in the previous Office Action mailed 4/21/06.

Applicant's arguments, filed 8/23/06, have been fully considered, but have not been found convincing.

Applicant submits that the '321 patent teaches the use of cetyl myristoleate (CMO) and CMO compounds in combination with other compounds useful for treating inflammatory disease. Applicant argues that the '321 Patent is not even directed towards HMG or its involvement in proinflammatory cytokine release. Instead the '321 Patent focuses on the use of chemical compounds, not antibodies, for the treatment of inflammatory disease. Applicant submits that the '321 Patent does not provide any suggestion to combining a TNF antagonist, such as infliximab or etanercept, with an antibody that binds to an HMGB polypeptide to treat inflammatory disease. Further Applicant submits that the person of ordinary skill in the art would not have been motivated to treat a condition in a patient characterized by activation of an inflammatory cytokine cascade which comprises administering to a patient a composition comprising an antibody that can bind to an HMGB polypeptide and an agent that inhibits TNF biological activity such as infliximab, etanercept and others cited in the claims. Accordingly, Applicant concludes that the cited references fail to provide the suggestion and reasonable expectation of success, which are required to establish *prima facie* obviousness.

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Contrary to Applicant assertions, given that TNF inhibitors shown to be effective for short term treatment of inflammation such as RA as taught by the '321 Patent, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the infliximab or etanercept taught by the '321 patent with the anti-HMG1 antibody taught by the Wang in a method of treating a condition in a patient characterized by activation of an inflammatory cytokine cascade and further to use a human, humanized, chimeric, single chain, or fab fragment antibody taught by the '223 patent. Obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). MPEP 2143.02.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 6, 2006

Maher Haddad
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